REMARKS

Status Summary

A request for continued examination, filed April 7, 2003, was entered. Claims 60, 65-69, 71-72, and 80-99 are under examination. The remaining of claims 1-99 were canceled previously. Claims 68, 82-83, 86-88, and 93-99 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that does not enable one skilled in the art to practice the invention. Claims 66 and 68 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claims 60, 65-69, 71-71, and 80-99 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over the documents of record. The drawings are refused entry. Reconsideration in view of the following remarks is respectfully requested.

Entry of the Drawings

The Office of Petitions has dismissed a petition for entry of new drawings (Figures 1-4). Official action, page 2, item 3. **The decision on petition notes that the appropriate avenue for entry of the drawings is via submission to the examiner for review as not disclosing new matter. The examiner has failed to respond to the request, instead simply referencing the decision on petition.**

New Figures 1-4 were submitted with the last-filed response and entry of the figures was requested. An affidavit by Dr. Hariharan was submitted with the petition, which attested that replacement Figures 1-4 contain the same subject matter as described in the specification as filed. **Applicants respectfully request that the examiner consider entry of the drawings as directed by the decision on petition.**

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claims 68, 82-83, 86-88, and 93-99 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that does not enable one skilled in the art to practice the invention. In particular, the examiner states that C2B8 and Mab 24-31 must be readily available to the public or obtainable by a method set forth in the specification. The examiner also states that amendment of the specification to identify deposit information is required and request confirmation that the term "IDEC-C2B8" refers only to the deposited material of claims of U.S. 5,843,349. Official action, pages 3-4, item 4. This rejection is respectfully traversed.

The antibody designation "IDEC-C2B8" is alternately used to describe RITUXAN® (rituximab). *See* Business Wire press release July 16, 1997 (enclosed). Cells expressing the RITUXAN® (rituximab) antibody are publicly available as deposit number 69119 from the American Tissue Type Collection (ATCC). In support thereof, a receipt issued by the ATCC to confirm receipt of the deposit is submitted herewith. Applicants have amended the specification to identify the deposit. In addition, the complete sequence of the rituximab antibody is disclosed in U.S. Patent No. 5,736,137. The examiner's attention is directed to Figures 3A-3F of the '137 patent, wherein the tandem chimeric antibody expression vector further comprising murine light and heavy chain variable regions is disclosed, which sequence corresponds to anti-CD20 in TCAE 8 as deposited.

With respect to the Mab 24-31 antibody, U.S. Patent No. 6,001,358 does not provide enablement of the Mab 24-31 antibody in that only variable region sequences appear to be disclosed. Official action, page 4, item 4. Applicants respond that the examiner improperly contests claim validity of an issued patent.

Every patent is presumed enabled. 35 U.S.C. § 282. The question of validity of invalidity is reserved to the courts. In particular, examiners are precluded from comment as to the validity or invalidity of any claim in any U.S. patent, except as necessary for examination of a reissue application, a reexamination proceeding, or an interference proceeding. MPEP § 1701.

Claim 1 of the '358 patent is directed to humanized antibodies, or antigen-binding fragments thereof, which specifically bind the CD40 ligand and which comprise the disclosed variable light chain and variable heavy chain sequences of the Mab 24-31 antibody. None of the above-noted exceptions merit the examiner's comment as to validity of the claims of the '358 patent, which are presumed valid. The use of the antibodies of the '358, as now claimed, are therefore enabled.

In addition to the foregoing, which applicants believe fully enables practice of the invention, Mab 24-31 was deposited with the American Type Culture Collection (ATCC) on September 1994 and was assigned deposit number HB 11712. A copy of the deposit receipt is attached. The specification is also amended to identify the deposit.

As yet another source for obtaining the 24-31 antibody, Research Diagnostics Inc. offers the 24-31 antibody for sale to the public as item # RDI-CD40L-2431. *See* attached product information sheet.

Based on the foregoing, this rejection of claims is believed to be rendered moot, and withdrawal of the rejection of claims 68, 82-83, 86-88, and 93-99 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 66 and 68 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite with respect to the antibody designations "IDEC-C2B8" and Mab 24-31." Official action, page 4, item 5. This rejection is also traversed.

Claim 60 does not include reference to either of the above-noted antibody designations. As this rejection applies to claims 82, 83, 86, 93, 95, and 97, applicants clarify that "C2B8" is not a trade name. The examiner notes that this rejection shall be withdrawn upon such clarification.

With respect to Mab 24-31, applicants reiterate that Mab 24-31 is known in the art and publicly available from Research Diagnostics Inc. as item # RDI-CD40L-2431. *See* enclosed product information sheet. Thus, claims 68, 82, 83, 87, 88, and 93-95 are believed to be sufficiently distinct to meet the requirements of § 112, second paragraph.

Rejection of Claims Under 35 U.S.C. § 103(a)

Claims 60, 65-69, 71-71, and 80-99 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,287,537 to Kaminski et al. (Kaminski) and/or U.S. Patent No. 5,843,439 to Anderson et al. (Anderson) in view of Smiers et al. (1996) *Br. J. Hematol* 93:125-30 (Smiers), Schattner et al. (1998) *Blood* 91:2689-97 (Schattner), Gruss et al. (1997) *Leukemia and Lymphoma* 24:393-422 (Gruss), Renard et al. (1996) *Blood* 87:5162-70 (Renard), U.S. Patent No. 6,001,358 to Black et al. (Black), and U.S. Patent No. 5,747,037 to Noelle et al. (Noelle). The examiner also relies on U.S. Patent No. 5,686,072 to Uhr et al. (Uhr) as teaching that chemotherapuetic treatments and combination therapies were known in the art. The examiner merely reiterates previous arguments with respect to the above-noted references. In the view of the examiner, a skilled artisan would have had motivation and expectation of success in treating leukemia using anti-CD20 and anti-CD40L antibodies and standard chemotherapeutic methods. The examiner dismisses applicants' previously submitted arguments as an attempt to attack the claims individually when the rejection is based on a combination of references. Official action, pages 5-8, item 7. This rejection is respectfully traversed based on the arguments set forth below.

The examiner bears the burden of presenting a *prima facie* case for obviousness, which requires: (1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) the teaching or suggestion of all the claim limitations of the applicant's invention in the combined prior art references; and (3) a reasonable expectation of success. MPEP § 2143. In the instant case, the examiner has not met this burden on the following basis: (1) failure to individually consider the claims in view of each of the cited references; (2) failure to identify a specific suggestion or motivation to perform the presently claimed invention; and (3) improper use of an "obvious to try" standard.

I. The Rejection is Unclear as to Which Reference(s) Apply to Which Claim(s)

The Manual of Patent Examining Procedure (MPEP) instructs that a plurality of claims should never be grouped together in a common rejection unless equally applicable to all claims in the group. MPEP § 707(d). Notwithstanding this instruction, the examiner has grouped all pending claims into a common obviousness rejection in view of nine references. A brief review of the claims and the cited references reveals that all nine references are equally applicable to each of the claims.

In view of the examiner's grouping of claims together in a common obviousness rejection, it is difficult if not impossible for applicants to address the merits of the rejection on a claim-by-claim basis. MPEP § 706.03 (j) states: "It is important for an examiner to properly communicate the basis for a rejection so that the issues can be identified early and the applicant can be given fair opportunity to reply." Therefore, applicants respectfully request that if the examiner is not persuaded by the additional arguments herein and intends to continue applying some or all of the ten references to the claims in another rejection, then the examiner should do so in the form of another non-final office action to give applicants a fair opportunity to address the merits of the rejection.

II. The Cited References Lack A Specific Suggestion Or Motivation To Perform The Claimed Combination

With regard to the first of the above-noted factors to establish a *prima facie* case of obviousness, suggestion or motivation to combine, such motivation may be found "where there is some teaching, suggestion, or motivation ... either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the

art." MPEP § 2143.01 (citing *In re Kotzab*, 217 F.3d 1365, 1370 55 USPQ2d 1313, 1317 (Fed. Cir. 2000)). In a proper analysis of obviousness, the level of knowledge of one with ordinary skill in the art cannot be substituted for a clear suggestion to make a combination. *See A-Site Corp. v. VSI International Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). Not only must such motivation be present, "there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant." *In re Dance,* 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (emphasis added) (citing *In re Raynes,* 7 F.3d 1037, 1039, 28 USPQ2d 1630, 1631 (Fed. Cir. 1993); *In re Oetiker,* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992).

The fact that the prior art teaches individual elements of the claimed invention that are generally known or within the capabilities of one with knowledge in the art is not, however, sufficient to establish a *prima facie* case of obviousness without any specific teaching or suggestion for making the combination. Therefore, the examiner is required to show how and why the applicants would have been motivated to combine the references in the manner combined by the examiner. Though the motivation to combine prior art does not have to be expressly stated in the references themselves, "the examiner must present a convincing line of reasoning" for a proper conclusion that an invention is obvious in view of prior art. *See In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). *See also, Ex parte Clapp,* 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). When relying on a "scientific reasoning" rationale for combining references, the examiner must provide evidentiary support for the existence and meaning of that scientific theory. *See, In re Grose,* 592 F.2d 1161, 201 USPQ 57 (CCPA 1979).

The present invention provides methods for treating B cell lymphoma via administration of an anti-CD20 antibody having B cell depleting activity in combination with an anti-CD40L antibody. This specific combination therapy is not identified or suggested as a useful therapy for B cell lymphoma in the cited references.

With regard to the examiner's contention that the applicants have improperly argued the references individually, the cited position of the MPEP does not obviate the requirement, set forth by the Federal Circuit, that a combination of references can be used to support a rejection of claims as obvious *only* upon showing a suggestion or motivation to make the *specific* combination claimed. In addition, the examiner has failed to identify a explicit suggestion in the prior art to combine the references or to provide the requisite evidence of a scientific rationale for combining the references.

The examiner separately relies on subsets of the cited documents to support individual therapies (*i.e.*, administration of B cell depleting anti-CD20 antibodies for the treatment of B cell lymphoma, and administration of anti-CD40L antibodies for inhibition of B cell proliferation). The further relies on Uhr, which suggests that two different anti-B cell antibodies may be useful for cancer therapy, as providing motivation and expectation of success for the claimed combination therapy. The examiner's explains that "the anti-B cell antibodies taught by Uhr et al. affect cell cycle, which, in turn, would be similar to the use of anti-CD20 or anti-CD40L antibodies which affect B cell or B cell leukemia cell proliferation." Uhr clearly lacks a specific suggestion to practice the claimed invention. As noted above, a proper analysis of obviousness, the level of knowledge of one with ordinary skill in the art (*i.e.*, that any unnamed combination of antibodies may be made, as suggested by Uhr) cannot be substituted for a clear suggestion to make a combination. *See A-Site Corp. v. VSI International Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). The examiner has failed to demonstrate motivation for making the specific combination therapy now claimed, and thus a *prima facie* case of obviousness has not been made.

III. The Examiner Has Improperly Used An Obvious To Try Standard

The Federal Circuit has consistently held that "obvious to try" is not to be equated with obviousness under 35 U.S.C. § 103. *See e.g., In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). The end result of a pursuit is not obvious simply because it may be obvious to try to achieve such a result. In the instant case, the examiner has improperly relied on an "obvious to try" standard to thereby conclude that the cited documents teach (1) anti-CD40L therapy for B cell lymphoma, and (2) the claimed combination therapy for B cell lymphoma, which includes administration of both anti-CD20 antibodies and anti-CD40L antibodies.

The examiner relies on the combined teachings of Schattner, Gruss, and Renard as teaching "the importance of CD40L-mediated interactions in B cell leukemia and clinical manifestation . . . CD40:CD40L interactions are par[t] of cellular activation and neoplastic tumor cell growth which would be useful for the therapeutic management of CD40+ tumors." Official action, at page 7, ¶ 6. The examiner cites Smiers as teaching that B cell leukemias express both CD20 and CD40. Official action, at page 7, ¶ 2. As noted above, the examiner appears to rely on this subset of cited references as allegedly teaching that anti-CD40L antibodies can be used for the treatment of B cell lymphomas. Official action, at page 7, ¶ 7.

Applicants respond that the combined teaching of the cited references is at best a proposal to try the combination, given that none of the above-noted references disclose use of an anti-CD40L antibody for B cell lymphoma therapy.

Given the absence of workable methods for treating B cell lymphoma via administration of an anti-CD40L antibody, as above, the examiner's further extrapolation to arrive at the now claimed combination therapy also fails. Again, the examiner's proposed combination of cited documents is at best a invitation to try the combination, which is an improper standard for determining obviousness. Any perceived ease or ensured success in such combination is flawed, given potential adverse interactions when employing combination therapies and the persistent difficulty in treating cancer. The claimed combination therapy is not obvious simply because one may try *any* combination of existing therapeutic antibodies.

Based on the foregoing arguments, applicants believe that the cited documents do not render obvious the combination therapy of claims 60-65, 71-72, and 80-99. Thus, applicants respectfully request that the rejection of claims under § 103(a) be withdrawn.

Provisional Rejection of Claims
Based on Obviousness-Type Double-Patenting

Claims 60, 65-69, 71-72, and 80-99 are provisionally rejected under the doctrine of obviousness-type double patenting in view of the claims of co-pending U.S. Application No. 09/772,938. Official action, page 9, item 8. Applicants respond that a terminal disclaimer will be filed when one or more claims in the instant application are in condition for allowance.

Conclusion

All objections and rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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December 31, 2003

TAC/JBM:ntb

VIEW IN FRAME

BUSINESS WIRE

Other Issues

(BW) IDEC Pharmaceuticals Receives Notices of Allowance for Additional Patent Protection Covering Rituxan and Provax

BUSINESS WIRE - 44 Montgomery St, 39th Floor, San Francisco, CA 94104; Tel: (415) 986-4422; FAX: (415) 788-5335 - Wednesday, 16 July 1997.

SAN DIEGO, California--(BW HealthWire)--July 16, 1997--IDEC Pharmaceuticals (Nasdaq:IDPH) today announced the receipt of notices of allowance for three **United States** patents.

The first allowed patent covers the company's IDEC-C2B8 (rituximab) antibody, now known as RITUXAN(TM), which is the subject of Biological License Applications (BLAs) filed in February 1997 with with the U.S. Food and Drug Administration (**FDA**). A counterpart European patent covering RITUXAN was granted in 1996. The second and third allowed patents cover the PROVAX(TM) adjuvant composition of matter and expand on the patent allowed in 1995 covering methods of using PROVAX to safely induce specific cell-mediated cytotoxic T-cell responses in humans and animals.

"The anti-CD20 antibody patent further enhances and solidifies the already strong patent estate surrounding our lead product, RITUXAN," said William R. Rohn, IDEC's senior vice president, commercial operations. IDEC and its development partner, **Genentech**, Inc. have completed a Phase III clinical trial with RITUXAN. The proposed indication is for the treatment of relapsed or refractory low grade or follicular non-Hodgkin's B-cell **lymphoma**. The BLAs for RITUXAN are scheduled for review by the FDA's Biological Response Modifiers Advisory Committee on Friday, July 25, 1997.

"The additional U.S. patents on our PROVAX technology are commensurate in scope with the granted European patent and provide broad composition of matter protection for our formulation in combination with any antigen," said Nabil Hanna, IDEC's senior vice president, research and preclinical development. "Additionally, the third patent provides specific protection for the PROVAX/papillomavirus antigen formulation for use as a therapeutic vaccine against condylomas and cervical carcinomas." IDEC is currently in discussions with other companies for licenses to PROVAX.

IDEC Pharmaceuticals focuses on developing targeted therapies for the treatment of cancer and autoimmune diseases. IDEC's products act chiefly through immune system mechanisms, exerting their effect by binding to specific, readily targeted immune cells in the patient's blood or lymphatic systems.

IDEC Pharmaceuticals' press releases are available at no charge through Business Wire's News on Demand Plus. For a menu of IDEC's current press releases and quarterly reports or to retrieve a specific release, call 888/329-2309. On the internet see http://www.businesswire.com/cnn/idph.htm and http://www.shareholdernews.com/idph .

The statements made in this press release contain certain forward looking statements that involve a number of risks and uncertainties. Actual events or results may differ from the company's expectations. In addition to the matters described in this press release, timelines for clinical ongoing activity are subject to change, results of pending or future clinical trials cannot be accurately predicted and decisions by the FDA and other regulatory agencies, as well as the risk factors listed from time to time in the company's SEC filings, including but not limited to its Annual Reports on Form 10-K for the year ended December 31, 1996, and Form 10-Q filed May 13, 1997, may affect the actual results achieved by the company.

IDEC Pharmaceuticals is a registered U.S. trademark and RITUXAN is a U.S. trademark of the company. The company headquarters is located at 11011 Torreyana Road, San Diego, CA 92121.

CONTACT: IDEC Pharmaceuticals, San Diego Connie Matsui, 619/550-8656

Keywords: CLINICAL TRIAL; PAPILLOMAVIRUS; IMMUNE SYSTEM; CLINICAL TRIALS

970716
BW970712

American Type Culture Collection

12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 898-853 ATCCNORTH • FAX: 301-770-1587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

T : (Name and Address of Depositor or Attorney)

Dartmouth Medical School
Attention: Randolph J. Noelle
640 W. Borwell Building
Dartmouth Medical School
1 Medical Center Drive
Lebanon, NH 03756

Deposited on Behalf of: Trustees of Dartmouth College

Identification Reference by Depositor:	ATCC Designation
Mouse hybridoma IgG1 anti-human CD40 Ligand (gp39), 24-31	HB 11712
Mouse hybridoma IgG1 anti-human CD40 Ligand (gp39), 89-76	HB 11713

The deposits were accompanied by: __ a scientific description __ a proposed taxonomic description indicated above.

The deposits were received September 2, 1994 by this International Depository Authority and have been accepted.

AT YOUR REQUEST:

X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your resp nsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested September 8, 1994. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person h ving authority to repr sent ATCC: _____ Date: September 9, 1994

Annette L. Bade, Director, Patent Depository

cc: Amy E. Mandragouras

rev: June 11, 2003

HOME (index HOME page)

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CD CLUSTERED ANTIBODIES

(anti-Human and others as indicated)

NOTE: Please inquire for bulk or custom formulations (without preservative or carrier).

Research Diagnostics Inc offers a wide line of antibodies. Since no one antibody works best for all applications (flow cytometry, neutralization, blotting, histochemistry, ELISA, etc), we offer many different types of antibodies to help solve this problem. Please inquire for other applications or types of antibodies not listed below. All products are for in vitro research use only-not for use in or on humans or animals-not for use in diagnostics. Price/availability/specifications subject to change without notice.

CD154 (CD40 Ligand) Antibodies

Mouse anti-human CD154 antibodies

-3 clones & polyclonals

CATALOG#	CLONE#	Workshop	Host	Form	Price
RDI-CD40L-2431	24-31	VI	mIgG1	purified	$325.00
RDI-CD40L-2431FT	24-31	VI	mIgG1	FITC	$375.00
RDI-CD40L-2431BT	24-31	VI	mIgG1	Biotin	$375.00
RDI-CD40L-2431PE	24-31	VI	mIgG1	PE	$500.00
RDI-CD154abm-TP	Trap-1	VI	mIgG1	purified	$325.00
RDI-CBL543	B-B29	VI	mIgG2a	purified	$350.00

-see also rabbit and goat anti-CD40L antibodies -see below.

-see also recombinant human CD40-Ligand Antigen in our cytokine section

DATA SHEET: mouse anti-human CD 40L (gp39) clone 24-31

Catalog#: RDI-CD40L-2431 $325.00/vial

Also available conjugated to FITC: #RDI-CD40L-2431-FT $375.00/100T

also available Biotin conjugated cat#RDI-CD40L-2431BT $375.00/100ug

also available PE conjugated: cat#RDI-CD40L-2431PE $500.00/100T

Package Size: 100ug in 100ul (1mg/ml) 50mM sodium phosphate pH 7.5, 500mM Potassium Chloride, 150mM NaCl, 0.5mg/ml Gentamicin Sulfate (preservative).

Species: mouse IgG1

Antigen: human sgp 39 fusion protein

Purity: >95% immunoglobulin by SDS-PAGE. Purified from low FBS containing tissue culture supernatant using Protein A. Product contains <1% bovine immunoglobin.

LOT# see sheet with shipment

CLONE: 24-31

Activity: Reacts with human CD40L. This antibody immunoprecipitates a CD40L (gp39) molecule of 36 kd. The antibody will stain activated CD3+human PBL and will functionally block MLR, sgp30 induced B cell proliferation and T cell dependent B cell differentiation.

Application: -Indirect fluorescence (approx 0.8ug/500K cells) -Briefly, ficoll prepared human peripheral white blood cells were stimulated by incubating 6 hours at 5 million cells/ml in RPMI 10% FBS media including 3ug/ml phytohemagglutinin-P and 1ng/ml Phorbol 12- Myristate 13-acetate. 500K cells were then washed and incubated 45 minutes on ice with 80ul of product at 10ug/ml. Cells were washed 2X and incubated with 50ul of secondary antibody and then washed 3X. A net of 5% of population of the cells stained positive with a mean shift of 306 fluorescent units compared to the IgG1 negative control.

-Blocking experiments-MLR (mixed Lymphocyte Response) can be blocked using approx 10ug/ml when 300K human PBL's(responders) are cultured with 100K irradiated allogenic human PBL's (stimulators). Inhibition can be observed by day 5 when using a 3H thymidine pulse to monitor proliferation. B cell differentiation induced by activated T cells and Il-2 can be measured by Ig production of IgD+ naive B cells.

Monoclonal anti-CD40L significantly inhibits this Ig production at levels of 1-10ug/ml.

-titers must be determined for each application

Storage: Store at 4 Deg C. DO NOT FREEZE.
Precautions: For In vitro research Use Only. Not for use in or on humans or animals or for diagnostics.

References: Dr. Randolph J. Noelle, Dartmouth Medical School

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